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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,423	05/02/2007	Kazuhiro Chiba	2060.8	7066

7590 11/16/2009

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EXAMINER	
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ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
11/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,423	CHIBA, KAZUHIRO	
	Examiner	Art Unit	
	KATHERINE ZALASKY	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 4-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 4-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 2 and 4-8, as amended 4 August 2009, are currently pending. **Claims 1 and 3** are cancelled.

Claim Rejections - 35 USC § 103

1. **Claims 2 and 4-8** are rejected under 35 U.S.C. 103(a) as being unpatentable over Chiba et al. (JP 2003-183298) in view of Chiba et al. (JP 2003-062448, both references are combined/translated in US 2007/0066799) and Kortenaar et al. (Rapid and efficient method for the preparation of Fmoc-amino acids starting from 9-fluorenylmethanol).

Regarding **claim 2**, Chiba et al. '799 discloses a method of separating a reaction product generated by reaction of a first substance and a second substance (abstract), comprising the steps of:

(a) mixing the reaction product with a hydrocarbon temperature-sensitive carrier residing in a liquid-phase state ([0075], cyclohexane with soluble carrier dissolved therein mixing with Fmoc-Val solution at room temperature, heated to form homogeneous solution)

(b) fixing an anchor region of the reaction product to the hydrocarbon temperature-sensitive carrier by converting the hydrocarbon temperature-sensitive carrier to a solid-phase state by changing temperature of a reaction system ([0075], reaction solution was cooled and the cyclohexane layer, with the soluble carrier bonded with Val-NH_2, was separated, [0046], may be separated as a solid)

(c) removing impurities from the reaction system ([0075], [0046])

(d) releasing the anchor region of the reaction product from the hydrocarbon temperature-sensitive carrier by converting the hydrocarbon temperature-sensitive carrier to a liquid-phase state by changing temperature of the reaction system ([0046], separated solid is heated to vaporize and remove cyclohexane, leaving only the desired peptide product)

wherein the first substance has an anchor region capable of being fixed to the hydrocarbon temperature-sensitive carrier (soluble carrier region, Scheme pg 5-6) and a reaction region that reacts with the second substance (NH_2 group, Scheme pg 5-6), and wherein the hydrocarbon temperature-sensitive carrier is reversibly changed from a solid-phase state to a liquid-phase state by a change in temperature ([0043], [0046]), which fixes the anchor region in the solid-phase state and does not fix the anchor region in the liquid-phase state ([0075], [0076], [0046] becomes a homogeneous solution when heated which allows peptide product to be separated).

While the reference does not explicitly disclose the step of reacting the first substance with the second substance to generate a reaction product, the reference does disclose that Fmoc-Val is mixed with carrier material. Fmoc-Val is the reaction product of the free amino acid and an Fmoc derivative (as taught by Kortenaar et al., pg 399/C1, "General procedure for the preparation of Fmoc-amino acids"). Therefore, the step of reacting valine and the Fmoc derivative is inherent in the method of the reference. Further, while the reference does not explicitly disclose that the anchor region is introduced into the reaction product through the reaction between the first and

second substances, the anchor region (the portion of the amino acid reacting with the soluble carrier is made available to bond with the soluble carrier as the reaction product prohibits the opposing side, in this case with the amino group, from bonding with the soluble carrier). Therefore, the anchor region is defined by the reaction of the first and second substances.

Regarding **claim 4**, Chiba et al. '799 discloses a method of separating a complex generated by interaction of a first substance and a second substance (abstract), comprising the steps of:

(a) mixing the complex with a hydrocarbon temperature-sensitive carrier residing in a liquid-phase state ([0075], cyclohexane with soluble carrier dissolved therein mixing with Fmoc-Val solution at room temperature, heated to form homogeneous solution)

(b) fixing an anchor region of the complex to the hydrocarbon temperature-sensitive carrier by converting the hydrocarbon temperature-sensitive carrier to a solid-phase state by changing temperature of a reaction system ([0075], reaction solution was cooled and the cyclohexane layer, with the soluble carrier bonded with Val-NH_2, was separated, [0046], may be separated as a solid)

(c) removing impurities from the reaction system ([0075], [0046])

(d) releasing the anchor region of the complex from the hydrocarbon temperature-sensitive carrier by converting the hydrocarbon temperature-sensitive carrier to a liquid-phase state by changing temperature of the

reaction system (Figure 1, pg 294/C2, “Plasmid Elution and Determination of DNA Content”, re-dissolved in buffer on ice, addition of 0.15M NaCl elutes plasmid into liquid, heating to 60 ºC precipitates biopolymer, which is removed by centrifugation)

wherein the first substance has an anchor region capable of being fixed to the hydrocarbon temperature-sensitive carrier (soluble carrier region, Scheme pg 5-6) and an interaction region that interacts with the second substance (NH_2 group, Scheme pg 5-6) and wherein the hydrocarbon temperature-sensitive carrier is reversibly changed from a solid-phase state to a liquid-phase state by a change in temperature ([0043], [0046]), which fixes the anchor region in the solid-phase state and does not fix the anchor region in the liquid-phase state ([0075], [0076], [0046] becomes a homogeneous solution when heated which allows peptide product to be separated).

While the reference does not explicitly disclose the step of interacting the first substance with the second substance to generate a complex, the reference does disclose that Fmoc-Val is mixed with carrier material. Fmoc-Val is the reaction product of the free amino acid and an Fmoc derivative (as taught by Kortenaar et al., pg 399/C1, "General procedure for the preparation of Fmoc-amino acids"). Therefore, the step of reacting valine and the Fmoc derivative is inherent in the method of the reference. Further, while the reference does not explicitly disclose that the anchor region is introduced into the reaction product through the reaction between the first and second substances, the anchor region (the portion of the amino acid reacting with the soluble carrier is made available to bond with the soluble carrier as the reaction product

prohibits the opposing side, in this case with the amino group, from bonding with the soluble carrier). Therefore, the anchor region is defined by the reaction of the first and second substances.

Regarding **claims 2 and 4**, Chiba et al. '298 discloses everything cited above (machine translation, [0007], [0020]-[0022]), but does not explicitly disclose that the anchor region is released from the carrier by changing the temperature. However, Chiba '448 discloses that when cyclohexane is in a solid form with a desired product, the product may easily be separated out by heating the solid to release the product and evaporate the cyclohexane (machine translation, [0014]). Therefore, it would have been obvious to one having ordinary skill in the art to solidify and separate the cyclohexane and peptide product from the solution, once the peptide synthesis is complete, and then heat the solid until the cyclohexane is evaporated off in the method of Chiba et al. '298, as taught by Chiba '448, since doing so provides a purified, isolated peptide product which is free of solvent.

Regarding **claims 6 and 8**, Chiba et al. '799 discloses all of the claim limitations as set forth above. Additionally, the reference discloses the method wherein the hydrocarbon temperature-sensitive carrier is cyclohexane ([0043]).

Regarding **claims 5 and 7**, Chiba et al. '799 discloses all of the claim limitations as set forth above. While the reference does disclose that cyclohexane is a preferred hydrocarbon temperature-sensitive carrier and that the solvent may also be chosen from the group of alkanes, cycloalkanes, alkenes, alkynes or aromatics ([0043]), the reference does not explicitly disclose that the temperature-sensitive carrier is a C_{10}-C_{30}

hydrocarbon. However, the reference does teach that cyclohexane is preferred because it has a melting point of about 6.5ºC ([0043]). With this teaching, one of ordinary skill in the art may also look to use additional organic solvents of alkanes, cycloalkanes, alkenes, alkynes and aromatics which have melting points near this value. Since cycloalkanes are most desired ([0043]), one may be drawn to cyclooctane (MP 10-14.8ºC), cylcononane (MP 11ºC), cyclodecane (MP 10-11.9ºC) or cyclotridecane (MP 24.45ºC), among other similar options (MP data provided in Knovel Critical Tables, see pgs 1-11). Additionally, if one of ordinary skill in the art were to choose a solvent with a higher melting point, such as cyclodecane or cyclotridecane, it would take less energy to solidify the mixture since it would not be necessary to cool the temperature to 6.5ºC or below.

Response to Arguments

2. Applicant's arguments with respect to **claims 2 and 4** have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

3. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE ZALASKY whose telephone number is (571) 270-7064. The examiner can normally be reached on Monday-Thursday, 7:30am - 6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KZ/
10 November 2009

/Krishnan S Menon/
Primary Examiner, Art Unit 1797